



Infant and Environmental Exposures to Thimerosal and Neuropsychological Outcomes at Ages 7 to 10 Years

CDC conducted the *Infant and Environmental Exposures to Thimerosal and Neuropsychological Outcomes at Ages 7 to 10 Years* study to investigate possible associations between prenatal and early childhood exposure to thimerosal-containing vaccines and/or immunoglobulins and deficits in neuropsychological functioning. Thimerosal is a preservative that contains ethyl mercury and is used in some vaccines and immunoglobulins. This study was not designed to assess possible association between thimerosal and autism.

This study was designed to improve upon previous studies that assessed the possible association between ethyl mercury exposure from thimerosal-containing vaccines and neuropsychological functioning including an objective measurement of neuropsychological functioning. These improvements reduced the potential for study biases.

The study was further strengthened by engaging a panel of independent external consultants to advise on the study design, selection of the neuropsychological test battery, interpretation of results, and editing of the draft manuscript. The consultants have expertise in the fields of toxicology, epidemiology, biostatistics, vaccine safety, and also included a representative from the autism advocacy community. The external consultants provided their individual input into the study protocol and the analysis plan.

The study evaluated 1,047 children between the ages of 7 to 10 years who received vaccines during the 1990s when thimerosal was used as a preservative in many childhood vaccines. The study used a retrospective cohort design. Computerized medical records were used to select a sample of children with a wide range of exposures from thimerosal-containing vaccines and immunoglobulins during infancy. Each child's level of exposure to ethyl mercury was determined through a review of electronic immunization registries, medical records, personal immunization records, and parent interviews. Each child was then administered a series of standardized neuropsychological tests in a clinical setting at ages 7 to 10 years.

The study found only a few statistically significant associations between exposure from thimerosal and neuropsychological functioning. The weight of the evidence from this study does not support an association between early ethyl mercury exposure from thimerosal-containing vaccines and/or immunoglobulins and neuropsychological functioning at ages 7 to 10 years.

Resource Materials

The following technical reports are extended versions of the manuscript and describe all of the

various analyses conducted in this study. These documents allow for a more complete presentation of methods and results than was possible within the space constraints of the scientific article, "[***Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years***](#),"* by Thompson et. al.

- [Download the complete Technical Report Volume I](#) (PDF-1.5MB)
- [Download the complete Technical Report Volume II](#) (PDF-9.7MB)

The [Public Use Data Set](#) from the *Study of Prenatal and Infant Exposure to Thimerosal and Neuropsychological Outcomes at Ages 7-10 Years* is available by mail request through CDC's Office of Immunization Safety.

Terms You Should Know on This Page

Thimerosal (ethyl mercury) is a preservative that has been added to some vaccines because it is effective in killing bacteria and in preventing bacterial contamination.

Methyl mercury is a chemical that is often found in some fish and exposure primarily occurs by eating fish.

Neuropsychological testing is a procedure that measures and identifies cognitive impairment and functioning in children and adults.

Early childhood is the period between birth and seven months (1 to 214 days).

Frequently Asked Questions

What is the purpose and design of this study?

This study is a follow up study to the Vaccine Safety Datalink (VSD) thimerosal screening analysis (Verstraeten et. al., 2003), and addresses inconsistent results from that screening study regarding associations between neuropsychological delays and thimerosal exposure. This study examines associations between thimerosal exposure through vaccination and immunoglobulin preparations and the following neuropsychological outcomes:

- Speech and language skills
- Executive functioning/attention
- Fine motor coordination
- Perceptual organization
- Motor tics
- Academic functioning
- Intellectual functioning
- ADHD symptomatology

This study recruited children from May 2003 to May 2004 who, in their first year of life, could have been immunized with vaccines containing thimerosal. The children were between the ages of 7 and 10 years at the time of the study. The study design included the administration of a battery of standardized neuropsychological tests administered by trained testers who were blinded to the

children's thimerosal exposure; the addition of medical chart abstractions and immunization records provided with the permission from biological mother to ensure complete and accurate immunization data; and the collaboration of external expert consultants in development of the study protocol, monitoring of study conduct, interpretation of findings, and review of final publication.

Will this study answer questions about a possible association between thimerosal exposure through vaccination and autism?

This study does not assess autism as a possible outcome of thimerosal exposure through vaccination. Autism occurs too infrequently to be assessed with the study design used in this neurodevelopmental study. CDC is conducting a separate study to specifically evaluate possible associations between thimerosal and autism.

What methods were used for this study?

This retrospective cohort study was performed with extensive assessment of thimerosal exposures and neuropsychological functioning. This included a rigorous review of computerized and paper medical records, personal immunization records, and maternal interviews to assess exposures to thimerosal through vaccines and immune globulins.

To assess neuropsychological functioning, a battery of tests was administered by trained assessors in a clinical setting. The outcomes measured included speech and standard language, verbal memory, achievement, fine motor coordination, visual spatial ability, attention and executive functioning, behavior regulation, tics, and general intellectual functioning. In addition, information was collected from parents and teachers about attention, hyperactivity and executive functioning.

The safety concerns regarding thimerosal exposure is based upon the hypothesis that cumulative exposures to ethyl mercury through vaccines could result in neuropsychological disorders and deficits. Biological samples for the participants were not taken for this study. Rather, the source of the child's ethyl mercury exposures were obtained through parent interviews, review of medical records and immunization registry information. Because infants excrete significant amounts of mercury in their stool after vaccinations, biological samples obtained at ages 7 to 10 years would not have provided more accurate information.

How was this study design strengthened over earlier studies?

This study employed several methods to address limitations identified in earlier thimerosal studies:

- To reduce potential selection and health care seeking biases, children were selected independent of their health status and each child was assessed independent of thimerosal exposure and health care seeking behaviors.
- A comprehensive and objective assessment of each child's neuropsychological functioning was conducted using a battery of standardized neuropsychological tests. Most of these tests were administered in a clinical setting by trained professionals.
- Extensive information was collected about each child's medical history, maternal prenatal fish consumption (a source of methyl mercury) and socioeconomic and educational factors that

could have influence on the child's health and development.

What were the limitations to this study?

The major limitations include:

- A majority of the families selected refused to participate or could not be located.
- The study could not control for interventions, such as speech therapy, that could have reduced potential negative effects of thimerosal exposure.
- Some of the data collected was based on a mother's recall of information during her pregnancy 7 to 10 years earlier such as fish consumption during pregnancy, which may have resulted in some erroneous associations.

What are the major findings from this study?

A total of 378 statistical tests were conducted. Each child was tested on 42 neuropsychological outcomes, 3 exposure periods and the full model plus gender specific analyses. Among the 42 outcomes measured, the study found that the majority of the outcomes had NO association with thimerosal exposure and most associations would be what is expected by chance alone.

Only a few statistically significant associations or consistent patterns between exposure to thimerosal and neuropsychological functioning were found.

- Among males, increased prenatal exposure was associated with significantly better performance in visual spatial ability (Stanford Binet Copying test), and poorer performance with attention and executive functioning (WISC III Digit Span Backward Recall test). There were no significant associations for females.
- Increased exposure from birth to 7 months of age was associated with significantly better performance among males on achievement (WJ-III: Letter-Word Identification test) and among females on fine motor coordination (Grooved Peg Board Non-Dominant Hand test) and attention and executive functioning (WISC III Digit Span Backward Recall test). Among males, higher exposure was associated with poorer performance with attention and executive functioning (Brief Parent Rating of Behavioral Regulation test), and a higher likelihood of motor and phonic tics reported by the child assessor were observed.
- Among males, higher exposures during the first 28 days of life had beneficial associations with improved performance on fine motor coordination (Finger-Tapping-Dominant-Hand and the Finger-Tapping-Non-Dominant-Hand tests), and general intellectual functioning (WASI Performance IQ test). Among females, higher exposure was associated with poorer scores on one test of verbal intellectual functioning (WASI Verbal IQ) and a lower likelihood of motor tics reported by parents were observed.

The weight of the evidence in this study does not support a causal association between early mercury exposure from thimerosal-containing vaccines and/or immunoglobulins and neuropsychological functioning at ages 7 to 10 years.

Who are the expert consultants CDC is collaborating with on this study?

The independent consultants represent a broad spectrum of expertise in fields related to child development, immunization, and immunization safety, as well as a representative from the autism advocacy community. The resulting study is better informed by this broad expertise, and potentially more credible to the larger public because of the external input.

The consultants provided input into the development and revision of the study protocol and analysis plan, and many of the consultants volunteered to provide comments on the study results and the final manuscript.

Related Links

Questions & Answers: Thimerosal in Seasonal Influenza Vaccine

Thimerosal is a very effective preservative that has been used since the 1930s to prevent contamination in some multi-dose vials of vaccines.


NIAID-Supported Studies on Mercury, Thimerosal, and Vaccine Safety

National Institute of Allergy and Infectious Diseases (NIAID) fact sheet on vaccine safety and mercury.

Institute for Vaccine Safety*

Johns Hopkins Bloomberg School of Public Health provides an independent assessment to help guide decision makers and educate physicians, the public, and the media about key issues surrounding the safety of vaccines.

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Page Located on the Web at

http://www.cdc.gov/od/science/iso/research_activities/thimerosal_outcomes.htm

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